Sources of Mercury Exposure to Children in Low- and Middle-Income Countries

Rita Ann Kampalath[1]; Jennifer Ayla Jay[2]

1 Geosyntec Consultants, Los Angeles, CA, U.S.A.
2 Civil and Environmental Engineering Department, U.C.L.A., Los Angeles, CA, U.S.A.

Corresponding Author:
Rita Ann Kampalath
Geosyntec Consultants
3415 S. Sepulveda Blvd, Ste 500
Los Angeles, CA 90034

Tel: +1 (310) 451-1500
Fax: +1 (310) 496-1902
kampalath@gmail.com

Background. Many children in low- and middle-income countries face enhanced risks of exposure to contaminants via the environment, parental occupation, and other routes. While mercury (Hg) is a global pollutant whose transport properties allow it to have an impact even in pristine areas, the presence of significant Hg sources in the developing world can cause localized effects that are more severe than those observed in other areas.

Objectives. This paper provides a narrative review of sources of Hg exposure to people in the developing world with a particular focus on children, and presents an overview of key aspects to this important issue.

Methods. We searched Web of Knowledge and Google Scholar using keywords including combinations of "mercury" and one or more of the following: "children," "exposure," "breast milk," "artisanal mining," "prenatal," "religion," "medicine," "dental amalgam," "chlor-alkali," "VCM," "vaccine," "e-waste," "industry," "beauty," "cosmetics," "strategies," "child labor," "costs," and "developing countries" to find peer-reviewed articles pertaining to Hg exposure in the developing world.

Results. Sources of Hg exposure include mining, consumption, industrial operations, religious practices, traditional medicines, beauty products, vaccines, dental amalgams, and waste scavenging and recycling.

Conclusion. Children in the developing world are often subject to higher levels of Hg exposure than those living in developed countries due to the higher prevalence of Hg-intensive industrial processes and consumer products, lack of environmental regulation, and limits in mobility and food choices, among other factors. This issue can be addressed through additional research to fill in data gaps on exposure sources, establish sound and enforceable policies, and increase education and participation in affected communities. Challenges to addressing this problem include limited resources for needed equipment, training, and manpower to implement solutions.

Competing Interests. The authors declare no competing financial interests.

Keywords. mercury, children, exposure, developing countries, low-income countries, middle-income countries, artisanal gold mining

J Health Pollution 8: 33–51 (2015)

Introduction

As a result of factors such as lack of regulation and resources, and the use of outdated technology and materials, people in low- and middle-income countries are often exposed to environmental pollution through routes and to degrees that are generally not present in the developed world. It has been estimated that 20% of the total burden of disease in the developing world is due to environmental pollution.[1]

Mercury (Hg) is no exception to this trend. Over time, there has been a shift in the origin of anthropogenic Hg emissions, primarily driven by economic growth, although a number of the most Hg-intensive activities are also prevalent in or nearly exclusive to low- and middle-income countries, notably artisanal small-scale gold mining. As a result, emissions in low- and middle-income countries have increased, with approximately 40% of global anthropogenic emissions to air now coming from Southeast and East Asia. Emissions in Sub-Saharan Africa and South America are slowly rising, and now account for approximately 16% and 13% of global anthropogenic emissions-to-air, respectively. Simultaneously, emissions from North America and Europe are in decline and now account for approximately 13.5% of global anthropogenic emissions.[2]

In general, children are often at a greater risk than adults for exposure to environmental pollution due to their smaller size, behaviors (e.g., putting hands and objects in the mouth) and the vulnerability of their still-developing systems. Depending on the chemical form of Hg, exposure can occur through inhalation or consumption, and can impact a number of the major bodily systems, including the nervous system, kidneys, lungs, gastrointestinal tract, skin, and cardiovascular system.[3] As some of the major sources of global Hg exposure are concentrated in low- and middle-income countries (e.g. mining) and because of the higher susceptibility of children to deleterious effects from Hg exposure, this review will discuss the major routes of Hg exposure in low- and middle-income countries – consumption, industrial operations, and mining—with a focus on impact to children, as well as strategies to mitigate these sources.

Abbreviations	
ASGM	Artisanal and small-scale gold mining
BAER	Brainstem auditory-evoked responses
etHg	Ethylmercury
EU	European Union
Hg	Mercury
IQ	Intelligence quotient
MeHg	Methylmercury
NGO	Non-governmental organization
PDI	Psychomotor development index
RfD	Reference dose
TCVs	Thimerosal-containing vaccines
UNEP	United Nations Environment Program
UNGMA	United Nations Global Mercury Assessment
USEPA	United States Environmental Protection Agency
VCM	Vinyl chloride monomer
WHO	World Health Organization
μg/g	Micrograms per gram
μg/L	Micrograms per liter

Background

The Nature of Mercury

Hg is the only metal that may be found in a gaseous, liquid, or solid state at standard temperature and pressure. Some of the most stable and common forms of Hg are elemental Hg, Hg(0), which is typically in a gaseous or liquid state, inorganic divalent Hg, Hg(II), which is often bound to ligands such as chloride, sulfide, or organic matter, and methylmercury (MeHg). Once released, Hg(0) is stable enough to be transported globally, and therefore may be found even in areas with little or no local Hg sources. Climate change may increase this global transport through higher temperatures and altered wind patterns.[9] In the atmosphere, Hg(0) may undergo a number of reactions, including oxidation to Hg(II). In terrestrial and aquatic environments, inorganic Hg(II) may undergo methylation to form MeHg, CH_3Hg^+, the most toxic of the stable forms due to its ability to bioaccumulate and biomagnify. For Hg, the type and severity of health effects are dependent on the form and concentration of Hg to which the individual is exposed.

Effects on Humans

In general, Hg exposure in low- and middle-income countries and to children specifically may occur through several routes, including consumption (typically in the form of MeHg) of fish, breast milk, or other food products containing high levels of Hg, occupational exposure in areas with artisanal gold mining (typically in the form of Hg(0)), and medical use. Exposures due to accidents and other consumer products also occur.[3,10,11]

As previously stated, children are considered to be particularly vulnerable to environmental contaminants in general due to a variety of factors, including differences in uptake, excretion, and sensitivity due to their developmental stage. Specific stages are particularly critical in terms of vulnerability to environmental contaminants, such as the pre-conception, gestation, and postnatal periods.[3,12,13] In addition, children's typical behaviors (such as touching various surfaces, playing on the ground, putting their hands in their mouths) may also increase their chemical exposure relative to adults. Infants have a particularly high vulnerability to Hg poisoning due to highly efficient gastrointestinal absorption, propensity to accumulate rather than excrete Hg from brain cells, and immature detoxification mechanisms.[13]

Neurodevelopmental issues are a hallmark of Hg exposure. A study that qualitatively assessed the effects of MeHg exposure on neurological development in Amazonian children living in gold-mining communities found negative correlations between hair Hg concentrations and performance on the copying component of the Stanford-Binet, which involves copying two-dimensional geometric designs with pencil and paper.[14] Children with higher hair Hg concentrations (> 10 μg/g) were found to make more errors than children with low levels (< 1 μg/g). A recent study also showed that children with higher levels of Hg in cord blood (>11.4 μg/L) were more likely to be diagnosed with attention deficit hyperactivity disorder.[15]

In general, the systems most affected by Hg exposure are the central nervous system (all forms), kidneys (primarily elemental and inorganic), lungs (primarily elemental), skin (primarily elemental and inorganic), gastrointestinal tract (primarily inorganic), and cardiovascular system (primarily organic).[3] Previous reviews have discussed the health effects of Hg exposure in detail.[3,10,16]

Although to date no threshold has been officially established where no developmental effects are observed after MeHg exposure[10], the effects of low levels of exposure are less clear. There is some evidence that even low levels of prenatal exposure may result in early childhood neurocognitive effects.[17] The following sections will discuss common sources of Hg exposure to people, particularly children (including the prenatal period) in low- and middle-income countries.

Sources of Hg

Currently, a variety of anthropogenic sources comprise 30% of the total annual emissions of Hg to air. Natural sources of Hg, including volcanoes and wildfires, account for 10% of the total, while re-emissions of previously released Hg, most of which is likely from anthropogenic sources, constitute 60% of the total.[2] The latest United Nations Global Mercury Assessment (UNGMA) estimated new (as opposed to re-emitted) annual anthropogenic emissions at approximately 1,960 metric tons (uncertainties resulted in a range from 1,010 to 4,070 metric tons), with 24% of contributions coming from coal burning, as Hg can be present as a trace element in coal.[4] Artisanal and small-scale gold mining activities (ASGM), which are frequently conducted with little emissions control and occur almost entirely in low- and middle-income countries contribute 37% of new emissions to air.[4,5]

Hg is also frequently present as an impurity in copper, zinc, lead, gold, and nickel ores. As a result, increases in non-ferrous metal production are a significant contributor (12%) to increases in Hg releases to the atmosphere, particularly in low- and middle-income countries.[4] Other important sources include: cement production (9%), consumer product waste disposal (5%), large-scale gold production (5%), and contaminated sites (4%).[2,4] Hg is also present in a number of products that people interact with on a daily basis, including electrical and electronic switches, fluorescent light bulbs, thermostats, thermometers, and batteries.[6] In terms of the origin of Hg releases, nearly half of global anthropogenic emissions come from China and India (40% from Southeast and East Asia, and 8% from South Asia).[2,7,8] Overall, the UNGMA reports that Hg emissions peaked in the 1970s, followed by a decline over the following 2 decades. After having been relatively stable, there is some evidence of a recent increase. Most current estimates predict that Hg emissions in 2050 will be higher than current levels.

Methods

Due to the extensive research that has been conducted to date on this topic, this paper does not attempt to comprehensively discuss every study that has been published, but is rather a narrative review presenting an overview of key aspects to this important issue. We used the search engines Web of Knowledge and Google Scholar with keywords including combinations of “mercury” and one or more of the following: “children,” “exposure,” “breast milk,” “artisanal mining,” “prenatal,” “religion,” “medicine,” “dental,” “beauty,” “cosmetics,” “strategies,” “child labor,” “costs,” and “developing countries” to find peer-reviewed articles pertaining to this topic. Literature searches using specific countries and continents as keywords (Brazil, the Philippines, China, India, Indonesia and Africa) were conducted as well. Reference lists from papers identified through these literature searches were also reviewed for additional literature. Particular focus was placed on papers that were heavily cited (greater than 20 times), that had been published within the last 10 years, or that presented relevant data on otherwise un- or understudied topics or regions. Reports from governmental and non-governmental agencies (NGOs), and the United Nations (including the World Health Organization [WHO]) were also reviewed.

Key Sources of Mercury Exposure

The following sections discuss several of the key sources of exposure to Hg in the developing world, namely mining, consumption, and industrial activities, as well as other notable but less significant sources.

Mining

Mining of metals is one of the most significant sources of anthropogenic Hg emissions in the world.[2] In large-scale mines, Hg is still mined as a primary product in a few low- and middle-income countries, including Algeria, Kyrgyzstan, and China.[18] Although active Hg mining is now limited, with only 1 mine in Kyrgyzstan still exporting, many areas that formerly contained large-scale Hg mines are still heavily contaminated as a result of historical operations. Of particular note are the Guizhou Province in China, which has deposits that account for 60% of the Hg in China, and Huancavelica in Peru, which produced Hg for silver extraction from the Spanish colonial

(Top) Artisanal gold miners around the world often use mercury in the gold mining process. This activity is responsible for about 30% of mercury emissions worldwide
(Bottom) Children playing on ground contaminated by mining

period.[6,19,20] In addition, regulatory activities that address legal Hg mining activities may not address issues with illegal mining.

As described earlier, ASGM has been estimated to be the largest source of anthropogenic Hg emissions globally, followed by fossil fuel combustion, with activities concentrated in low- and middle-income countries.[2] This source has been estimated to account for 37% of global emissions to air.[5] Since gold preferentially binds to Hg, it is used in ASGM activities to form an amalgam with gold, which is naturally found in small quantities mixed in sediments and possibly bound to other elements such as sulfur. The Hg-gold amalgam may then be removed from the slurry, and the Hg often burned off using blowtorches or open flame. This allows gold to be recovered at low concentrations, since Hg emissions are typically not controlled nor collected for reuse. However, this process results in significant emissions of Hg(0). It has been estimated that for every gram of gold recovered through ASGM activities, 1 to 2 grams of Hg are released.[21] In addition, since these practices frequently occur close to water bodies where gold-containing sediments are collected, Hg is released into aquatic environments with a high potential for methylation.

Currently, ASGM is most often found in low- and middle-income countries in Asia, Africa, the Pacific, and South America, and constitutes a considerable health risk to the communities and particular families who take part in this practice. It has been estimated that some 10 to 15 million people worldwide, including 3 million women and children, are directly involved in ASGM.[5,22] Numerous studies have surveyed Hg levels in miners and communities surrounding ASGM operations, including (but not limited to) studies conducted in Brazil, Ecuador, Tanzania, Indonesia, the Philippines, Thailand, Zimbabwe, and Mongolia.[23-41] A number of these have looked at Hg levels in children and have found concentrations of Hg in hair, urine, and/or blood samples that may cause adverse effects.[5,25,28,31,42] Children may be exposed to Hg through ASGM activities by their parents due to Hg residue on workers' clothing, hair, and skin, food sources contaminated by increased Hg discharges into the environment, and through directly assisting with ASGM activities.[43] It has also been shown that Hg vapor inhaled by pregnant women may diffuse across the placenta and accumulate in fetal tissue.[10,44] A study conducted in French Guiana linked mild neurodevelopmental issues in children from Amerindian communities where ASGM activities were common with maternal hair Hg levels.[45]

One study conducted in the Philippines, where ASGM activities have been going on since the early 1980s, looked at Hg exposure in residential communities proximal to mining activities in Mindanao.[42] Elevated Hg levels were found in fish samples, and in both water and sediment samples in rivers up to 15 km downstream from mining areas. In a study of 162 schoolchildren in the area, 10 children were identified as having elevated total Hg levels in their blood, with 1 child having elevated levels of MeHg in hair.

In a study of a gold mining community in Nambija, Ecuador, children with high blood and hair Hg levels were found to score significantly lower on a neurocognitive test.[31] In this community, another study focused on children of gold miners, who often help their parents in gold mining operations, significant differences were found in brainstem auditory-evoked responses (BAER) as compared to a control group, suggesting that these children may be at risk for neurodevelopmental issues.[32] Grandjean, et al. examined 351 children between ages 7 and 12 in Brazil, and found correlations between hair Hg concentrations and performance on tests of motor function, attention, and visuospatial abilities.[25]

In another study conducted by Bose-O'Reilly, et al., 166 children in Indonesia and Zimbabwe who resided in ASGM communities, some of whom worked directly with Hg themselves, were examined.[35] The children ranged in age from 9 to 17. Mercury levels in blood, urine, and hair were all found to be significantly higher in the study group as compared to a control group, with the highest concentrations found in children that worked with Hg directly. Typical signs of Hg intoxication were observed, including excessive salivation, complaints about metallic taste, ataxia, and discoloration of gums.

Consumption

The primary route of exposure for MeHg, the most toxic stable form of Hg, is consumption.

Fish

Fish is most frequently implicated as the source, although there have been several notable cases of organic Hg poisoning resulting from consumption of seeds treated with Hg-containing fungicides.[46,47] Due to the ability of MeHg to bioaccumulate and biomagnify in the food web, predatory fish, as well as fish caught in water bodies contaminated with Hg, tend to have the highest MeHg concentrations. Certain cooking methods, particularly deep frying, may exacerbate this issue by concentrating Hg.[48,49]

One of the most famous epidemiological studies on Hg exposure was conducted in the Faroe Islands,[50] where consumption of pilot whale meat, containing high MeHg concentrations, is the major source of MeHg exposure. In a study of approximately 600 children assessed at age 7, significant associations were found between poor performance on neuropsychological tests and cord-blood Hg levels.

In a study by Akagi, et al., fish consumption was implicated as contributing significantly to elevated levels of total Hg and MeHg observed in schoolchildren.[42] Another study in the Amazon found that while there are a number of different sources of Hg in the environment, hair Hg levels seemed to be most heavily influenced by fish consumption frequency as opposed to other factors such as gender or age.[51]

One study looked at 170 Amerindian women in the Bolivian Amazon region, where there are limited options for protein sources.[52] This study found significant relationships between fish consumption and Hg levels in hair. Significant relationships were also found between high hair Hg levels (>5 µg/g) and certain neurological issues (paresthesia and disturbances in balance).

High fish consumption by pregnant or breastfeeding women may pose a health risk to developing fetuses as well. Hg exposure in utero can adversely affect infant development.[53,54] Given the same maternal fish consumption, Hg exposure during pregnancy may be greater than infant exposure during breastfeeding.

Concerns over exposure to MeHg must be balanced against the benefits of eating fish, however. In developed countries, where there are many options for protein sources, fish consumption advisories can be followed without sacrificing a healthy and balanced diet. This is more of a challenge in communities that rely on fish for subsistence, such as native communities in the Amazon and in North America.[55,56] For many people, a few food sources such as fish or rice may comprise a large fraction of the diet.[56,57] In addition, there is some debate regarding the effects of low levels of MeHg exposure as opposed to infrequent, high dose meals, particularly on developing fetuses. This issue is particularly complicated since exposures may have different effects depending on at what point in gestation the exposure occurs.[50]

Rice

Another staple typical for a number of low- and middle-income countries is rice, which may account for up to 80% of caloric intake in some regions.[58] Rice paddies may serve as a favorable environment for Hg methylation since anaerobic conditions may exist in soils which are frequently submerged with water.[59] Several studies, many of which were done in China, have reported elevated levels of MeHg in rice, suggesting that in Hg-polluted areas in these regions, rice may be the main route of exposure of MeHg to humans.[59-65] In addition, rice, particularly white rice, is not as rich in micronutrients that might counteract the deleterious health effects of MeHg as compared to fish.[66] Examination of exposure to Hg from rice consumption is needed, particularly in countries that, like China, have high levels of both Hg and rice consumption, as well as the potential impacts to children's health.

Breast milk

Several studies have shown that chronic exposure to MeHg may negatively impact fetal and infant neurodevelopment, particularly during gestation and lactation.[67–69] In general, mean levels of mercury in breast milk, which, similar to blood levels, reflect recent Hg exposure, are within the range of 0.5 to 7 µg/L worldwide (A study by Behrooz et al. 2012 provides a table of measurements of Hg in breast milk across different studies).[10,53,70] However, in areas where mothers are exposed to high levels of Hg, concentrations can be significantly greater, making breast milk an important route of Hg exposure for infants. For instance, a review of environmental and health assessments of gold mining areas in

Indonesia, Tanzania, and Zimbabwe found median levels of 1.87 µg/L of Hg in 46 samples of breast milk, with a maximum of 149 µg/L, and 14 of the samples exceeded 4 µg/L.[71] To put these numbers in context, in a study conducted in Sweden total Hg concentrations in breast milk ranged from 0.1 to 2 µg/L, which was calculated to correspond to an exposure ranging up to 0.3 µg/kg/d, or approximately half the tolerable daily intake for adults recommended by the WHO.[72]

In a recent Iranian study, Hg content was measured in 80 human milk samples from women not occupationally exposed to Hg, living in 3 regions of the country.[53] The average Hg concentration in breast milk in women living in the countryside of Tabriz, an industrial area with known metal contamination (sources include cement production, steel industries, and fungicides), was 0.86 µg/L, which was statistically significantly higher than levels measured in women in non-industrial Tehran (0.12 µg/L) and Noushahr (0.15 µg/L). In Tehran and Noushahr, fish consumption was found to be a significant factor affecting breast milk Hg levels.

A separate recent study, also from Iran, studied Hg in 93 pairs of mothers and breastfed infants in 3 coastal communities with high seafood consumption: Nowshahr, Nur, and Sari.[73] Mean Hg levels in hair were 3.55 and 1.89 µg/g in mothers and infants, respectively, and the 2 measurements were correlated with each other. The USEPA (United States Environmental Protection Agency) reference dose of 1 µg/g was exceeded in 82.7% of mothers and 61.2% of infants, and the WHO “threshold” dose of 5 µg/g was exceeded in 31% and 10.7% of subjects in each group, respectively.

Similar to fish consumption, however, the risks of Hg exposure from breastfeeding must be weighed against the potential benefits. In a number of low- and middle-income countries in particular, where waterborne illness pose a serious health risk, use of formula over breast milk has been linked to higher rates of infant mortality.[74] A study of 9,424 infants and their mothers in Ghana, India, and Peru found the risk of mortality in infants that were not breastfed to be 10 times greater than that of primarily breastfed babies and double that of partially breastfed infants. In 2006, a large outbreak of diarrhea occurred among children in Botswana which was linked in part to preparation of formula with contaminated water.[75]

Industrial Operations

In addition to mining, there are a few major industrial sources of Hg emissions, including fossil-fuel burning power plants, metal smelting (particularly zinc), the Hg-cell process in chlor-alkali plants, and production of vinyl chloride monomer (VCM). These industries can result not only in health impacts for workers who are exposed occupationally, but also for surrounding communities through Hg emitted in waste streams or as byproducts into the environment. For example, in the town of Wanshan, one of the largest Hg-mining areas in China, atmospheric Hg was measured up to 2–4 orders of magnitude higher than pristine areas in Europe and North America, and elevated levels of Hg have been found in all environmental media, as well as in animals and local crops.[60,76–78] The health impacts of these industrial uses, however, particularly on children living in communities in low- and middle-income countries that are in proximity to these sources, requires further study.[10]

Approximately 24% of worldwide anthropogenic Hg emissions come from combustion of coal, particularly combustion of coal in Asia.[2] Coal combustion in China during winter has been shown to measurably elevate Hg concentrations in air in some cities above global background levels.[79-81] With ASGM, the VCM process, which uses a Hg-containing catalyst, constitutes about 45% of the global demand for Hg.[6] Demand for polyvinyl chloride, which is made from VCM, is particularly high in countries with extensive building projects, with most production of VCM occurring in China.[6] Ren et al. estimated that approximately 3.7% of total Hg used in this process was released into the environment through waste and byproducts, although approximately 21.7% of the mass of Hg could not be accounted for.[82]

The chlor-alkali industry represents the largest intentional use of Hg in the world.[83] The Hg-cell process, which was invented in the late 1800s, is used in chlor-alkali plants to produce a number of different products, but most commonly sodium hydroxide. Issues with the Hg cells, as well as contamination of products with trace amounts of Hg, including food products such as high fructose corn syrup,[84] have led to the phasing out of this process in favor of other methods. However issues remain, particularly in low- and middle-income countries where industry is slower to adopt new, cleaner technology. While many plants have committed to phasing out use of this process, the majority of those that have not are located in low- and middle-income countries.[85]

As one of the longest standing Hg-intensive processes, the chlor-alkali industry has more studies on the health effects from Hg exposure as compared to the other industries noted above. Several studies have documented the health effects among workers in chlor-alkali plants that were attributed to occupational exposure to Hg vapor.[86–89] Data on the effects of chlor-alkali plants on surrounding communities, especially in children, however, is more limited, as are studies conducted in low- and middle-income countries. A study conducted in Romania, which examined fish caught in a reservoir impacted by wastewater from a chlor-alkali plant, found elevated levels of Hg with a mean value of 1.8 μg/g in fish muscle.[90] Hair concentrations of people (including children) consuming fish from this reservoir were also significantly greater than concentrations from people consuming fish from upstream reservoirs. A study conducted in Kazakhstan found levels of Hg ranging from 0.16 to 2.2 μg/g in fish caught in a lake and a river located near a former chlor-alkali plant, with the majority of the fish exceeding the USEPA human health criteria for Hg of 0.3 μg/g.[91] One of the few studies that looked at impacts on children was a study conducted in Spain, which found significantly higher concentrations of Hg in hair from children (age 4) living near a chlor-alkali plant, as compared to children who did not.[92] This difference remained significant after adjustments were made for fish intake and other variables, such as gender.

Other Routes

Aside from the major routes of Hg exposure mentioned above, there are several other routes common in low- and middle-income countries, but which require further study to determine their impact on health. These include certain medical equipment, religious practices, traditional medicines, beauty products, vaccines, dental amalgams, and waste scavenging and recycling.

Medical Equipment

Certain health care equipment that may contain mercury, specifically thermometers and blood pressure devices, may also be used in low- and middle-income countries. The mercury-containing versions of these devices have long since been phased out in the US and the European Union (EU), and phase-out efforts are now ongoing in low- and middle-income countries, in particular due to an initiative led by Health Care Without Harm and the WHO, followed by the Minamata Convention which set a goal of global mercury-free health care by 2020.[93,94]

Religious Practices and Traditional Medicine

Certain religious practices that may be present in Latino and Afro-Caribbean communities involve mercury, particularly in the elemental and inorganic forms. Examples include Santeria, Espiritismo, Palo, and Voodoo.[95–98] In the belief that these practices may protect against evil or bring good luck, adherents may carry Hg around, wear it in amulets, consume or inject it, or sprinkle it in their homes or cars, where children can be exposed.[95,98,99] The Hg used for religious practices is often sold in 10 gram units.[96] To put this number into context, thermometers, which are well known to cause significant levels of Hg vapor exposure when broken, typically contain less than 1 gram of Hg.[96] A case study has been published on Hg exposure in children from families that take part in these practices; however, further study is required to establish the extent to which this source may have an impact on children's health, as well as how widespread these practices are.[100]

Hg has also been known to be used in traditional medicines, including in Ayurvedic remedies.[101–103] In Ayurvedic products, heavy metals are typically intentionally added and seen as necessary for normal function of the body.[101] Though lead poisoning is probably most frequently reported, cases of Hg poisoning have also been noted.[104,105] In a study conducted in India, lead and Hg were found in 64% of Ayurvedic products tested.[106] While their use is believed to be widespread among both children and adults, similar to religious practices, the extent to which their use represents a significant source of Hg exposure to children requires further study.[101]

Beauty Products

Use of Hg salts in consumer products has largely been phased out; however, these compounds can still be found in skin-lightening creams and soaps, which are relatively popular in many low- and middle-income countries.[107,108] Hg is often the active ingredient in these creams, rather than a contaminant, and acts by inhibiting the formation of melanin.[109] Surveys conducted in Mali, Nigeria, Senegal, South Africa, and Togo reported regular use of skin lightening products by 25%, 77%, 27%, 35%, and 59% of women, respectively.[110] Use was also reported in approximately 38% of women surveyed in 2004 in China, Malaysia, the Philippines, and Korea, and in India, 61% of the market for skin care products has been found to consist of skin lightening products.[110,111] One study of bleaching creams from Mexico found levels up to 36,000 μg/g in one brand, and another study found the highest concentrations in creams from Thailand, Lebanon, and England, ranging from 1,281 to 5,650 μg/g.[107,112] In a study of 150 women in different border states in the U.S. who were using Mexican bleaching creams, 84% of the participants had Hg urine levels greater than 20 μg/g.[108]

A number of surveys and case studies have been published reporting observations of Hg toxicity linked to use of cosmetic products containing Hg, including indications that use during pregnancy may lead to Hg exposure to the developing fetus.[107,108,113-116] Several studies have reported application of these creams on children as lighter skin can represent higher status.[10] In a case study conducted among Balkan refugees of various ages who used a skin bleaching product, elevated levels of Hg were found in blood and urine.[117] Health impacts from this route of exposure, both to developing fetuses, as well as to children, is an area in need of additional study.[10]

Dental Amalgam

Information on the extent of the use of dental amalgams in low- and middle-income countries is limited, and in many countries the challenge with oral health services is lack of availability and affordability.[118] Dental amalgam can be an important source of Hg to children directly and through exposure to the mother, however. A number of studies have noted correlations between the number of maternal fillings and Hg concentrations measured in fetuses and infants.[116–120] For example, Hruba et al. found a correlation between blood Hg levels and numbers of amalgam fillings in children, though levels did not exceed thresholds believed to cause adverse health effects.[124] Maternal amalgam fillings were associated with higher Hg levels in breast milk ($p<0.001$) in a study conducted in Lenjan, Iran. Hg in breast milk was measured at 2.87, 5.47, and 13.33 μg/L, respectively, in women with no amalgam fillings, with 1–3 fillings, and with 4–8 fillings.[125]

Although it is clear that there is a link between number of fillings and Hg body burden, it has not been shown that this exposure constitutes a health risk. A major study conducted in the US, the New England Children's Amalgam Trial, sought to investigate whether linkages could be found between dental amalgam and neuropsychological function.[126-128] For a period of 5 years, this study annually tested 534 children, ages 6-10, living in urban and rural areas. Results of this study showed elevated urinary Hg concentrations in children with dental amalgams as compared to children with non-Hg containing dental fillings, but very few significant differences in tests of neuropsychological function, with differences being inconsistent in direction.[127] Renal function was also tested during this study, and no significant differences were found in average levels of renal biomarkers between children with and without Hg-containing amalgams.[128] A significant increase was observed in the prevalence of microalbuminuria in children with amalgams in the latter 3 years of the study; however, it was not clear whether this finding was random or if the effects that were observed would be permanent, and further study was recommended.

Another study of 507 children in Lisbon, Portugal, aged 8-10, looked at correlations between dental amalgams and various neurobehavioral effects through annual follow-up tests for 7 years.[129] Similar to the New England study, no significant differences were found in neurobehavioral assessments of nerve conduction velocity of children with dental amalgams as compared to children with non-Hg dental fillings.

Thimerosal

A common route of Hg exposure for children in low- and middle-income countries is vaccines preserved with thimerosal, an organomercurial compound (sodium ethyl-Hg thiosalicylate $C_9H_9HgNaO_2S$) containing 49.6% Hg by weight, in the form of ethyl-Hg. The amount of Hg typically ranges from 12.5 to 25 μg per dose, with infants receiving vaccines at the WHO recommended schedule receiving a cumulative dose of etHg up to 187.5 μg.[130,131] As a result, thimerosal-containing vaccines (TCVs) may constitute a significant source of Hg-exposure during infancy. It has been estimated that Hg-exposure through TCVs may represent approximately 50% of Hg exposure to an exclusively breastfed infant over the first 6 months of life.[132]

Similar to dental amalgams, however, studies have not established a link between long-term health impacts and these levels of exposure. Studies suggesting adverse neurodevelopmental effects associated with TCVs, reviewed in Dorea 2013, mostly concluded that there were no lasting effects, or that further study is required.[133,134] In contrast, aside from a localized hypersensitivity reaction observed in some individuals, the preponderance of studies have not shown a linkage between adverse effects and TCVs given in their recommended doses.[10,130,135-140] Furthermore, etHg appears to be significantly less toxic than MeHg, although, as with MeHg, the effects of low doses of etHg are unclear.[132,141] However, genetic differences appear to result in a wide variation in susceptibility to Hg among individuals. This suggests that 'safe' levels of etHg ingestion may be lower for individuals with certain predisposing genetic factors as compared to the general population, and reveals a need for targeted research looking into this issue.

Based on the uncertainty associated with exposure to low doses of etHg, the biological plausibility for adverse effects in susceptible infants, the potential for children given multiple doses of TCVs exceeding the USEPA's reference dose (RfD) for Hg for cumulative exposure, and the ability to provide a safe alternative, the use of thimerosal has been banned in many developed countries, including the United States and the European

Union.[132] Based on the lack of evidence showing adverse effects of TCVs, however, the World Health Organization considers Hg exposure via thimerosal to be safe, and others have recommended the continued use of TCVs, particularly in low- and middle-income countries where vaccine-preventable diseases are more prevalent, and safe and cost-effective alternatives are currently non-existent.[132,142] The stance of the WHO on thimerosal use has also been endorsed by the American Academy of Pediatrics.[143]

Waste Scavenging and Recycling

It has been estimated that 20-50 million tons of e-waste is generated annually worldwide, which may contain a number of different compounds, both of value and hazardous, including Hg.[144] Due to the high costs of handling and recycling, wealthy countries tend to landfill this waste or ship it to poorer countries where labor is cheaper and environmental regulations may be more lax.[145] This practice has been banned through the Basel Convention of 1992; exportation, however, continues through legal loopholes by countries that have not ratified the Convention and through other illegal routes.[146,147]

Children in low- and middle-income countries constitute a significant portion of the labor that performs this work.[148] Since this work is informal, exposure of children to Hg through this route has not been documented. Several studies have documented elevated levels of other heavy metals in communities living in proximity to e-waste facilities, however.[147] Additional studies should be conducted to determine the impacts of this industry to children's health, especially with regard to Hg.

Discussion

There are a number of direct routes of Hg exposure that disproportionately impact children in low- and middle-income countries. Many of these, including traditional medicine, religious practices, use of consumer products such as beauty products, and waste scavenging are in need of additional study to more accurately assess their significance as a source of Hg exposure. Waste scavenging and recycling, in particular, seem to have the most potential to be a significant source of exposure due to the scale of the practice.

While there is a paucity of data on costs related to Hg exposure, Spadaro and Rabl calculated a first estimate of the global impacts of Hg on intelligence quotient (IQ) and the associated costs.[149] As an alternative to a detailed model of Hg exposure pathways, they applied a comprehensive transfer factor, which is the ratio of ingestion dose to emission rate. They then applied estimates of IQ detriment as a function of blood Hg, and correlations between blood Hg and ingestion rate. To estimate the costs of a decrease in IQ per point, these authors took the average of values obtained by 5 studies, obtaining a cost of $18,000 (in 2005 terms) per IQ point in the United States. Costs per lost IQ point in other countries were calculated by multiplying the US value by the ratio of the per capita GDP for the country to the per capita GDP in the US (both adjusted for purchase power parity). Their analysis lead to a global average of $3,890 per lost IQ point, and a marginal cost of $1500/kg emitted on a global scale.

Building from this work, Sundseth et al. analyzed economic benefits achievable through reduced Hg emissions.[150] The current Hg emissions trajectory will result in an increase in Hg emissions from 2005 to 2020, which these authors calculate will result in annual costs of $3.7B based on lost IQ.[151] Reduced emissions scenarios can result in 50-60% decreases in emissions, with corresponding annual cost savings of approximately $2 billion (in 2005 terms). Furthermore, there are very important non-quantifiable impacts of Hg emissions, including loss of quality of life from health impacts not considered in the analysis. Additionally, there are significant co-benefits for the reduction of emissions, as control technologies are typically multi-pollutant.

Reduction Strategies

Strategies to reduce Hg exposure through certain consumer products, food consumption, industrial uses, and mining will be discussed in turn below.

Consumer Products

As noted above, further research is needed to assess the impact and significance of the usage of several Hg-containing consumer products. Impacts of, and possible alternatives to, the use of dental amalgams and TCVs have been more widely studied. As discussed in earlier sections, concerns have been raised over the health impacts of dental amalgams containing Hg; however, there remains considerable question about whether their use constitutes a health risk. This, in addition to their low cost, ease of use, and durability have resulted in their continued widespread usage and debate over whether they should be phased out where alternatives are impractical.[152–154] Releases of Hg into the environment due to the use of dental amalgam, which is approximately 50% Hg, have, however, been found to cause environmental contamination.[152] Recognition of the importance of oral care and the need for further development of alternatives to dental amalgam led the WHO and UNEP to recommend a 'phase-down' rather than a 'phase-out' of its usage.[94,118] The UNEP's Minamata

Convention recommended several measures for reducing usage of Hg-containing dental amalgam, including (but not limited to): nationwide programs to promote dental health and reduce dental cavities; promoting the use of cost-effective Hg-free dental restoration options; promoting further research and development of, as well as education on, the use of Hg-free dental restoration materials; encouraging insurance policies that favor the use of Hg-free alternatives; and promoting environmental practices in dental facilities to reduce releases of Hg.[94]

As discussed above, studies have not shown that TCVs by themselves constitute a health risk in terms of Hg exposure.[10] Although use of this preservative has been banned in developed countries as a precaution and due to uncertainties in particular with regards to more subtle neurodevelopmental effects of exposure to low levels of Hg, the risks and benefits of continued usage must be considered, and in particular in the context of low- and middle-income countries where environmental exposure to Hg is likely to be higher, and much higher rates of vaccine-preventable diseases exist.[10,132] Further research into alternative preservatives is prudent, as currently there is no alternative to thimerosal that is similarly cost effective and functionally effective in maintaining the stability, potency and safety of vaccines.[132,142,155] This was recognized in the recent Minamata Convention which negotiated world-wide bans on a number of Hg-containing products, but excluded TCVs from the ban.[94]

Consumption

Although consumption of food sources high in Hg constitutes the predominant route of exposure to the most toxic stable form of Hg, MeHg, this route is directly influenced by release of Hg into the environment by Hg-intensive processes, such as ASGM and industrial operations, and the production of Hg-containing products. Aside from reducing sources contributing to Hg-contaminated food sources (discussed further below), education of potentially affected communities may be effective at reducing exposure from consumption of food high in Hg. An analysis of the impact of a federal advisory on fish consumption released in the US that was directed at pregnant women found reductions in consumption of fish after the release of the advisory, suggesting that widespread dissemination of information may be effective at changing dietary behavior.[156] Due to the nutritional benefits of fish consumption, however, there has been much debate about the use of fish consumption advisories in many low- and middle-income countries.[157–160] One approach that may be effective in regions such as the Amazon that have high biodiversity has been to direct interventions at changing fish-eating habits to focus on less contaminated species, rather than at limiting overall fish consumption.[157,161,162] This approach was found to be successful in a village on the Tapajos River in Brazil, with observed reductions in hair-Hg levels although villagers continued to eat the same quantity of fish.[162] Community participation was also noted as an important component of this program.

Industrial Uses

Several large-scale industrial processes that use Hg or Hg compounds are currently being phased out. The UNEP Minamata Convention has set a phase-out date of 2025 and 2018 for chlor-alkali production and acetaldehyde production, respectively.[94] Demand for VCM, however, is on the rise and since there is currently no economically feasible alternative, demand is unlikely to abate in the near future.[6] However, the Minamata Convention has proposed measures to reduce the usage and release of Hg from this and other Hg-utilizing industrial processes (specifically sodium or potassium methylate or ethylate, and production of polyurethane), including (but not limited to): reducing the use of Hg in terms of per unit production; introducing measures to reduce emissions and releases into the environment; supporting research into Hg-free alternative processes; and banning the use of Hg 5 years after Hg-free processes have been established as technically and economically feasible.

With regards to industrial point sources of Hg emissions, including coal-fired power plants and boilers, smelting processes, waste incineration and cement production, the Minamata Convention measures are aimed at setting national policies on emissions controls, implementation of best available technologies for new facilities, and tracking emissions. A study by Chakraborty et al. evaluated the effect of several Hg control strategies on national emissions of Hg in India, specifically phasing out intentional Hg applications, sourcing coal based on Hg content, washing of coal, flue-gas desulfurization, recovery of Hg from zinc smelters, and recycling of intentionally used Hg.[163] This analysis found that the combined reduction measures could reduce emissions by approximately 50%, with the greatest impact caused by transitioning to low-Hg coal sources.

Mining

As discussed above, large-scale Hg mining operations are now limited to a few sites. Although it may be difficult to bring about an end to all Hg mining, especially illegal operations, decreasing demand for Hg by finding and implementing alternatives to Hg-intensive industrial processes and phasing out the use of Hg-containing consumer products may be the most effective way to minimize Hg mining.

In terms of ASGM activities, a number of strategies have been proposed to reduce Hg usage as well as child labor in this industry. The UNEP notes that reduction in usage is more likely to be accepted by miners themselves if it results in an increase or at least the maintenance of income.[164] Four approaches that are specifically named are: 1) saving costs by eliminating or reducing the need for Hg; 2) saving time through more efficient processing methods; 3) recovering more gold by improving extractions techniques; and 4) negotiating better prices for gold that is mined using good practices. Technical solutions to reduce the need for Hg and increase efficiency exist in all stages of the gold recovery process.[164] Improving the initial concentration step, during which gold deposits are separated from other minerals, through the use of various separation techniques, including sluices, magnets, or centrifuges, can reduce the need for downstream Hg use. During the processing and refinement process in which Hg is removed from the Hg-gold amalgam, one of the most popular strategies for mitigating exposure and release of Hg is the use of retorts, due to their simplicity, effectiveness, and low cost. These devices, which allow Hg to be captured and recycled, may reduce Hg emissions by 75-95%.[164] Fume hoods and the use of more pure "activated" Hg may similarly reduce Hg use and emissions during this step.

Complete elimination of the need for Hg during ASGM would be ideal, however, and there are several techniques to accomplish this. Gravity-only methods such as panning and sluicing may be used to take advantage of gold's high density. The efficiency of these methods is highly dependent on the equipment and type of ore used. Chemical leaching of gold using cyanide is another Hg-free method which can obtain high recovery rates of up to 90% and is inexpensive. Although cyanide is also a hazardous substance, it is highly degradable and not persistent in the environment. However, misuse and poor management of cyanide in small-scale operations could result in serious health hazards and environmental impacts. Another Hg-free method of gold mining is the direct smelting, or 'borax method', in which gold is concentrated through panning or some other gravity method, and then heated with borax until melted. The gold then separates based on density and can be separated from the hardened slag. The efficiency of this method is dependent on use of an effective concentration technique, and is most competitive as a replacement for Hg methods in cases where small masses of concentrate are being processed due to the high energy cost of the melting step.[164]

A critical component to successful implementation of these techniques is education of exposed communities about the proper use and operation of Hg mitigation techniques and processes (particularly in the case of chemical leaching processes), as well as the risks of Hg-exposure. One study conducted in five sub-villages in Tanzania with a history of ASGM, with many residents who work as miners, looked at knowledge of the health risks of Hg exposure from ASGM operations.[165] It was found that approximately 41% of respondents were unaware of the health effects, with women being less knowledgeable than men (only 23% of women were aware of health risks). This is a concern since pregnant women should be particularly cautious with regards to Hg exposure. Artisanal miners with more awareness of the health impacts of Hg have been found to show more willingness to apply available workplace controls.[166]

Challenges

There are many challenges to reducing the impact of Hg on children in low- and middle-income countries. One major factor leading to greater risk for children in lower income countries is the economic necessity for children to participate in family occupational activities that can be Hg intensive; it has been estimated that up to one million young people are involved in artisanal mining worldwide.[35,167,168] The International Labour Organization has named artisanal gold mining one of the worst forms of child labor due to the arduous nature of the work and severity of the physical and chemical hazards, and featured this work in its 2005 World Day Against Child Labor.[169] Significant debate exists, however, over the best path to addressing this problem. Abolition of particular types of child labor can lead to children engaging in even less desirable forms of labor. In addition, many children work in order to provide themselves with educational opportunities that would not be possible without extra income for the family. For example, Okyere spent a 15-week period intensively studying child labor at an artisanal mining site in Ghana.[170,171] Many of the children interviewed reported that the reason they worked was to provide money for their schooling. Despite the policy in Ghana of cost-free schools, there are still many costs associated with education, including additional tuition fees, costs for textbooks, sports, activities, and transportation, and contributions to teachers' salaries. Over 40 of the children in the study worked to contribute to their families' incomes, and a few were the family's main breadwinner. Labor in ASGM was the means to accessing an education for children in this study, a phenomenon that has been observed elsewhere as well.[172] Clearly, in order for policy-based efforts to reducing child labor to be effective, the underlying problems of poverty and access to education must be addressed as well.

Conclusion

Hg exposure in children is a significant and increasing health problem throughout the developing world, with consumption of contaminated food sources and occupational activities as particularly important exposure routes. In many countries, multiple major sources of exposure exist, particularly where Hg-intensive activities such as ASGM lead to environmental Hg pollution which in turn lead to contaminated food supplies. Although the risks of Hg exposure are well known, in low- to middle-income countries the issue can be complicated due to lack of alternatives to major sources of exposure.

Addressing these sources will require a multi-pronged solution that includes additional studies to fill existing data gaps on the true magnitude of impacts from various sources, soundly developed and enforceable policies, and committed resources in the form of money, as well as equipment and trained staff. For sources such as artisanal gold mining, education and the support and involvement of the affected communities in decision-making will be necessary for successful implementation of solutions.[166] Policy-based efforts to alleviate Hg exposure from child labor should also address the underlying problems of poverty and lack of accessibility of education.

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